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Evaluation of knowledge, attitude and perceptions of future health care professionals on Japanese Encephalitis

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ABSTRACT

Background: Japanese encephalitis is a serious fetal disease that causes death. It is spread through an infected mosquito, especially in Asian and Pacific regions. The Japanese encephalitis virus (JEV) can cause severe inflammation of the brain. *Objective:* The current study's objective was to evaluate the knowledge, attitudes, and perceptions of future healthcare providers regarding Japanese Encephalitis from different medical institutes in Lahore, Pakistan. *Methods:* A cross-sectional, multi-centered observational study was conducted at multiple educational institutes. A structured self-made questionnaire was designed with knowledge, attitude, and perception-related questions. The study sample included 284 undergraduate students from the medical, dentistry, physiotherapy, and pharmacy departments. Data was collected from the respondents after they gave informed consent. The research project lasted 6 months. The collected data was analyzed through SPSS, utilizing descriptive and inferential statistics to summarize the results. *Results:* The knowledge of most future healthcare professionals as appropriate, as observed through baseline analysis. Healthcare providers know the name of Japanese Encephalitis but lack knowledge about its symptoms, preventive measures, and treatment protocols. *Conclusion:* The baseline evaluation of future healthcare professionals' knowledge was observed to be adequate. Moreover, attitude and perception were observed to be positive as well. Medical students presented appropriate knowledge, a positive attitude, and good perceptions comparatively. Educational programs should be conducted for undergraduate students to provide them with information about diseases. This will help them enhance their knowledge and improve practices regarding disease management and prevention.

Keywords: Attitude; Cross-sectional; Health care professionals; Japanese encephalitis; Knowledge; Practices; Undergraduate students.

1. INTRODUCTION

Japanese encephalitis is a fatal disease that is caused by the Japanese Encephalitis virus (JEV)- borne by mosquitos and is most prevalent in the regions of southern and eastern Asia (Van-Den-Hurk et al., 2009). JEV is a mosquito-borne infection transferred by mosquitoes of the Culex species (Culex tritaeniorhynchus group). The Flaviviridae family of viral pathogens is gathered under 3 groups: flaviviruses, hepaciviruses, and pestiviruses. Dengue virus, West Nile virus, Japanese encephalitis virus, yellow fever virus, and Tick-Borne Encephalitis Virus are the most known flaviviral infections. Eight species and two strains: St. Louis encephalitis, Japanese encephalitis, Murray Valley encephalitis, West Nile, Kunjin, Alfuy, Cacipacore, Yaounde, Koutango, and Ustusu viruses are present (Van-Den-Hurk et al., 2009). JEV is a single-stranded RNA gene of ~11 kb in length (Wang and Liang, 2015).

JEV is found in a zoonotic cycle; it can be enzootic and epizootic. JEV was found in the brain of a human encephalitis case in Tokyo in 1934 (Van-Den-Hurk et al., 2009). Prototype Nakayama strain was found in the brain of a patient with encephalitis (Tiwari et al., 2012). Flaviviruses history is about 10,000– 20,000 years old and four genotypes of (JEV) from genotypes I to III have been found (Solomon, 2003). Japanese Encephalitis is prevalent across South and Southeast Asia, surrounding an area bordered by Pakistan to the west, the Philippines and Japan to the east, and the Australian Torres Strait Islands to the south (Turtle and Solomon, 2018). The disease is epidemic along with obesity in different areas of Asia (Shahid et al., 2024). Different species of birds are reservoir hosts, while pigs are amplifying hosts (Mulvey et al., 2021).

The outbreaks of JEV in northern India and Nepal between 2005 and 2007 caused at least 11,000 reported cases (Van-Den-Hurk et al., 2009). The fatality rate in JE cases is 20%–30%, with psychiatric sequelae found in 30%–50% of survivors. Japanese encephalitis— the prospects for new treatments 50,000 cases and 15,000 deaths per year are due to JEV, particularly in rural areas of Asian countries (Solomon, 2003). JEV is the cause of human viral encephalitis, known as zoonosis, which is carried by culex mosquito bite. It is the root cause of acute encephalitis (Erlanger et al., 2009). It is induced by RNA flavivirus- a virus that affects the central nervous system (Solomon, 2003). It is a single filament-positive RNA virus that is associated with the family Flaviviridae (Kabilan et al., 2004).

The emergence of this disease emphasizes the presence of a link between humans and animals or birds in the atmosphere. It is the contributing factor of pediatric encephalitis or, in other words, pediatric viral encephalitis (Misra and Kalita, 2010). The outbreak of Japanese Encephalitis occurred in Japan in the year 1924 (Misra and Kalita, 2010). Afterwards, its outbreak occurred in Mainland China in the 1940s. Currently, 10,000-20,000 cases of Japanese Encephalitis are annually reported in China. Annually 2000-7000 cases of Japanese Encephalitis are reported in eastern and northern India on average. During the winter season, the JEV becomes inactive, but it is in its most active form during the summer and autumn seasons, which is why the outbreaks of JE depend on environmental temperature (Misra and Kalita, 2010).

Infection associated with the JE virus could be asymptomatic and begins as a nonspecific febrile sickness presented with aseptic meningitis, abortive type encephalitis, or fully developed encephalitis-like sickness. 5 to 15 days is a latent period of JEV. The start of sickness could be sudden, rapid, gradual, or progressive (Baluni et al., 2018). Symptoms may vary depending upon the region of CNS affected. However, the initial signs include undifferentiated febrile sickness, specifically stiffness and loose stools accompanied by altered consciousness, convulsion, light sensitivity, cephalalgia, retching, and psychosis in some cases. Subsequent symptoms consist of acute flaccid paralysis and Parkinsonism (Ghosh and Basu, 2009). Viral encephalitis is described by changes in behavior, impaired cognition, paroxysms, and brain dysfunction.

Lower limbs are less affected as compared to upper limbs. Local to bilateral seizures occur in acute encephalitis. In lethal cases, patients fall into a coma (Misra and Kalita, 2010). Virus isolation is the most common method to isolate JEV. In this method virus can be removed from the CNS followed by the spinal cord and blood (Roberts and Gandhi, 2022). The pharmacological management of JE includes corticosteroid therapy for an extended period of time (Gould et al., 2008). Mannitol infusion is used for controlling raised intracranial pressure (Karthikeyan et al., 2017). Use of routine antibiotics should be avoided if cerebrospinal fluid and imaging do not show infection (Turtle and Solomon, 2018). Interferon (INF-a) produced naturally in response to viral infections, causes blockage of release, assembly, and viral replication (Chakraborty et al., 2022).

Minocycline penetrates BBB because of good lipophilicity and also inhibits the 30S ribosomal subunit of bacteria. Paracetamol and acetaminophen should be used for fever (Gould et al., 2008). During the non-pharmacological treatment approach supportive care is proved to be effective for JE patients. Complications of JE result in enhanced mortality risk (Turtle and Solomon, 2018). Water intoxication and dehydration both must be avoided along with malnutrition. To prevent bed sores and respiration pneumonia, nursing care is of great importance (Kumar, 2014). Jaanese Encephalitis endemic areas prevent their exposure by taking appropriate safety by using insecticide repellents, wearing proper clothing, using permethrin-impregnated mosquito nets.

Japanese Encephalitis vaccines have been established since the 1950s and these include the Japanese Encephalitis vaccine [XIARO] and the chimeric vaccine (Gao et al., 2014). Lifestyle modifications and economic developments can prevent Japanese Encephalitis. By avoiding exposure to mosquitos, pigsties, and paddy fields and adopting new farming techniques. While there is no specific antiviral treatment for Japanese encephalitis, healthcare providers can provide supportive care to manage symptoms and complications. This may include intravenous fluids, medications to reduce fever and alleviate pain, and other supportive measures to ensure the patient's comfort and well-being (Gould et al., 2008).

Healthcare providers play a crucial role in preventing Japanese encephalitis through vaccination and public health measures. They can educate individuals and communities about the importance of vaccination, particularly in endemic areas where the risk of JE transmission is high (Ahmad et al., 2015). Additionally, they can provide guidance on personal protective measures such as using mosquito repellents, wearing protective clothing, and sleeping under mosquito nets, especially during peak mosquito activity periods (Srivastava et al., 2014). Healthcare providers are often on the frontline of disease surveillance, actively monitoring and reporting suspected cases of Japanese encephalitis to public health authorities. Timely reporting of cases helps in implementing control measures and preventing further spread of the disease (Hills et al., 2009).

2. METHODOLOGY

Study Design & Study Subjects

A multi-centered, cross-sectional observational study was conducted using a self-made questionnaire (SMQ) to evaluate the knowledge, attitude, and perception of future health care providers regarding Japanese encephalitis in Lahore, Pakistan. The data was collected using a quantitative research methodology involving a validated questionnaire with a consent form regarding Japanese Encephalitis.

Final-year undergraduate students were recruited for this study from different medical institutes of Lahore, Pakistan. A signed consent form was provided, and data was collected after consent to participate. The incomplete responses were excluded from the final study. Ethical approval from the Institutional Ethical Review Board and Bio-Ethical Committee (BEC) of Lahore University of Biological & Applied Sciences was attained with protocol approval number ERB-PHRMD-DPP/3219-B attributed to the present study.

Inclusion & exclusion criteria

The inclusion criteria for this research included final-year undergraduate students (future healthcare professionals) from different medical institutes, Medical, Dental, Physiotherapy, and Pharmacy departments, who willingly participated in the current study by signing the consent form. However, the students from health sciences departments belonging to 1st, 2nd, 3rd, and 4th year were excluded from the studies along with the passed-out students who were serving as healthcare professionals. Moreover, the students who were reluctant to participate in the present study were excluded.

Sample size

The sample size was calculated according to the convenient sampling technique. Approximately 300 students, both male and female, were approached for the data collection. 284 study subjects provided consent and were included in the present study. The study subjects were included from different medical institutions of Lahore, Pakistan, from four health sciences departments: medical, dentistry, Pharmacy, and Physiotherapy.

Study Setting & duration

The study settings of this research were multiple medical institutions in Lahore. The purpose of this study is to assess the knowledge, attitude, and perception among future healthcare providers from medical institutes in Lahore, Pakistan. The rapidly growing capital of Punjab is estimated to contain 11.3 million residents in accordance with 2017 survey. There are almost 16 private medical institutes in Lahore from which data was collected from future health care providers of different departments. The study duration was approximately 6 months.

Questionnaire Development

The questionnaire was divided into different sections regarding demographic factors, knowledge, attitude and perception regarding Japanese Encephalitis. The demographic section involved information on age, gender, faculty/ department, professional year, source of information, nationality, residence, and educational background. The knowledge section involved information about general knowledge regarding JE, the transmission of JE, a vaccine for the treatment of JE, and the prevention of Japanese encephalitis. The next section consisted of the attitude of students toward Japanese encephalitis. The last section is related to perception regarding JE, which involves the opinions and beliefs of students towards Japanese Encephalitis. The questionnaire was designed after an extensive literature review of the published research. After developing the questionnaire, the questions were subdivided into detailed and formal sub-questions.

Each question was reviewed to ensure it aligned precisely with our objectives, and any questions that elicited unnecessary or sensitive information were removed. Afterward, content validity was attained by sending it to 3 academicians who were experts; as a result of their suggestions, the questionnaire was modified and face-validated by checking on a small number of respondents. The pilot study was conducted on a small number of patients, and Cronbach's alpha values of 0.76, 0.71, and 0.73 were attained for the knowledge, attitude, and perception sections, respectively. The results of the pilot study were not included in the study's results. The first part of the questionnaire contained demographic information about the respondents, followed by 10 Knowledge questions, 10 attitude questions, and 10 perception questions. The cutoff points were decided based on 60% scores for appropriate knowledge, positive attitude, and good practices.

Statistical analysis

The data collected from the study subjects was analyzed and interpreted by using SPSS v21, IBM. Descriptive and inferential statistics were applied to summarize the variables. Categorical variables were presented as frequencies and percentages. To find factors regarding associations between independent variables, chi-square tests (Pearson chi-square) were applied, and where assumptions of chi-square analysis requirements were not met, Fisher exact tests were applied to calculate p-values. P-values less than 0.05 were considered statistically significant values.

3. RESULTS

The current study recruited 284 future healthcare professionals from different universities in Lahore, Pakistan. The majority of the study subjects were female, 64.4% with less than 30 years of age and belonging to the final year of medical, dental, physiotherapy, and pharmacy departments. Table 1 presents the demographic data of the respondents.

Table 1 Demographic Characteristics of study subjects (N=284)

#	Variables	Categories	Frequency (N)	Percentage (%)
1	Gender	Male	101	35.6
		Female	183	64.4
2	Age	< 30 years	279	98.2
		> 30 years	5	1.8
3	Department of future healthcare providers	Medical	71	25
		Dentistry	79	27.8

		Pharmacy	76	26.8
		Physiotherapy	58	20.4
4	Nationality	Pakistan	268	94.4
		Overseas	16	5.6
5	Resident	Day scholar	243	85.6
		Hostel	41	14.4
6	Healthcare professional in family	Yes	128	45.1
		No	156	54.9

The study was conducted to access the knowledge, attitudes, and perceptions of Japanese Encephalitis from the study subjects. The respondents were asked to provide information about their source of information about Japanese Encephalitis. The majority (47.2%) presented that the source of information for them was medical books, their course textbooks, and reference books, as demonstrated in (Table 2).

Table 2 Source of information of the study subjects

#	**Variables**	**Categories**	**Frequency (N)**	**Percentage (%)**
1.	Source of information about Japanese Encephalitis	Seminars/Workshops	48	16.9
		Research articles	90	31.7
		Medical Books (Reference/ Textbooks)	134	47.2
		Medical magazines	12	4.2

Table 3 presents the data regarding the knowledge, attitude, and practices of respondents regarding Japanese Encephalitis. It states that the majority of the respondents have appropriate knowledge of Japanese Encephalitis (62%), a positive attitude (60.2%), and a good perception (60.6%).

Table 3 Knowledge, attitude and practices of respondents regarding Japanese Encephalitis

#	**Variables**	**Categories**	**N (%)**
1.	Knowledge	Appropriate	176 (62%)
		Inappropriate	108 (38%)
2.	Attitude	Positive attitude	171 (60.2%)
		Negative attitude	113 (39.8%)
3.	Perception	Good perception	172 (60.6%)
		Poor perception	112 (39.4%)

Table 4 provides the association of demographic variables with respondent knowledge. Through statistical analysis, gender and age have no specific association with knowledge. However, the department of study subjects presented a significant statistical association with knowledge, demonstrating that medical students have the highest rates of appropriate knowledge comparatively. Table 5 provides the association of demographic variables with the respondent's attitude, presenting that the department of future healthcare professionals and the presence of healthcare professionals in the family have statistically significant associations with the respondent's attitude.

Table 4 The association of demographic variables with respondent's knowledge

#	Variables	Categories	Knowledge Category		p-value*	Effect size
			Appropriate	Inappropriate		
1	Gender	Male	58 (57.4%)	43 (42.6%)	0.241	-
		Female	118 (64.5%)	65 (35.5%)		
2	Age	< 30 years	172 (61.6%)	107 (38.4%)	0.402	-
		> 30 years	4 (80.0%)	1 (20%)		
3	Department of Future Healthcare Providers	Medical	53 (74.6%)	18 (25.4%)	<0.001	0.223
		Dentistry	59 (74.7%)	20 (25.3%)		
		Pharmacy	33 (43.4%)	43 (56.6%)		
		Physiotherapy	31 (53.4%)	27 (46.6%)		
4	The professional year of respondents	4th year	103 (60.6%)	67 (39.4%)	0.558	-
		5th year	73 (64.0%)	41 (36.0%)		
5	Nationality	Pakistan	165 (61.6%)	103 (38.4%)	0.565	-
		Overseas	11 (68.8%)	5 (31.3%)		
6	Resident	Day scholar	149 (61.3%)	94 (38.7%)	0.580	0.137
		Hostel	27 (65.9%)	14 (34.1%)		
7	Healthcare professionals in family	Yes	100 (78.1%)	28 (21.9%)	<0.001	0.301
		No	76 (48.7%)	80 (51.3%)		
8	Source of information about Japanese Encephalitis	Seminars/Workshops	32 (66.7%)	16 (33.3%)	0.546	-
		Research articles	52 (57.8%)	38 (42.2%)		
		Medical Books (Reference/ Textbooks)	86 (64.2%)	48 (35.8%)		
		Medical magazines	6 (50%)	6 (50%)		

*Pearson Chi-square test

Table 5 The association of demographic variables with respondent's attitude

#	Variables	Categories	Attitude Category		p-value*	Effect size
			Positive attitude	Negative attitude		
1	Gender	Male	60 (59.4%)	41 (40.6%)	0.837	-
		Female	111 (60.7%)	72 (39.3%)		
2	Age	< 30 years	169 (60.6%)	110 (39.4%)	0.352	-
		> 30 years	2 (40.0%)	3 (60.0%)		
3	Department of Future Healthcare Providers	Medical	48 (67.6%)	23 (32.4%)	0.002	0.046
		Dentistry	50 (63.3%)	29 (36.7%)		
		Pharmacy	32 (42.1%)	44 (57.9%)		
		Physiotherapy	41 (70.7%)	17 (29.3%)		
4	The professional year of respondents	4th year	99 (58.2%)	71 (41.8%)	0.406	-
		5th year	72 (63.2%)	42 (36.8%)		
5	Nationality	Pakistan	160 (59.7%)	108 (40.3%)	0.473	-
		Overseas	11 (68.8%)	5 (31.3%)		

6	Resident	Day scholar	153 (63.0%)	90 (37.0%)	0.021	0.137
		Hostel	18 (43.9%)	23 (56.1%)		
7	Healthcare professionals in family	Yes	115 (89.9%)	13 (10.2%)	<0.001**	0.548
		No	56 (35.9%)	100 (64.1%)		
8	Source of information about Japanese Encephalitis	Seminars/Workshops	32 (66.7%)	16 (33.3%)	0.286	-
		Research articles	47 (52.2%)	43 (47.8%)		
		Medical Books (Reference/ Textbooks)	84 (62.7%)	50 (37.3%)		
		Medical magazines	8 (66.7%)	4 (33.3%)		

*Pearson Chi-square test **Fisher exact test

Table 6 provides the association of demographic variables with respondent perception. Through statistical association, medical department students present good perceptions as compared to dental and physiotherapy students. However, pharmacy students obtained the lowest scores.

Table 6 The association of demographic variables with respondent's perception

#	Variables	Categories	Perception Category		p-value*	Effect size
			Good perception	Poor perception		
1	Gender	Male	57 (56.4%)	44 (43.6%)	0.290	-
		Female	115 (62.8%)	68 (37.2%)		
2	Age	< 30 years	168 (60.2%)	111 (39.8%)	0.370	-
		> 30 years	4 (80.0%)	1 (20.0%)		
3	Department of Future Healthcare Providers	Medical	51 (71.8%)	20 (28.2%)	<0.001	0.123
		Dentistry	53 (67.1%)	26 (32.9%)		
		Pharmacy	30 (39.5%)	46 (60.5%)		
		Physiotherapy	38 (65.5%)	20 (34.5%)		
5	Nationality	Pakistan	163 (60.8%)	105 (39.2%)	0.716	-
		Overseas	9 (56.3%)	7 (43.8%)		
6	Resident	Day scholar	144 (59.3%)	99 (40.7%)	0.274	0.137
		Hostel	28 (68.3%)	13 (31.7 %)		
7	Healthcare professionals in family	Yes	90 (70.3%)	38 (29.7%)	0.002	0.181
		No	82 (52.6%)	74 (47.4%)		
8	Source of information about Japanese Encephalitis	Seminars/Workshops	33 (68.8%)	15 (31.3%)	0.161	-
		Research articles	54 (60.0%)	36 (40.0%)		
		Medical Books (Reference/ Textbooks)	75 (56.0%)	59 (44.0%)		
		Medical magazines	10 (83.3%)	2 (16.7%)		

*Pearson Chi-square test

4. DISCUSSION

The present study observed the knowledge, attitude, and perceptions of the final-year students of the medical, dentistry, physiotherapy, and pharmacy departments. Japanese encephalitis is a fatal viral disease transmitted through a particular Culex species of mosquitos, that grow in standing water areas. The healthcare providers should have adequate knowledge regarding the disease to tackle the incidence of Japanese Encephalitis. However, future healthcare providers should be prepared to manage the cases be forehanded. The current study was conducted with the aim of accessing the knowledge, attitudes, and perceptions of future healthcare providers regarding Japanese encephalitis.

A total of 284 study subjects were recruited from the medical (25%), Dental (27.8%), Pharmacy (26.8%), and physiotherapy (20.4%) departments. Most of the study subjects were female, 64.4% with less than 30 years of age (98.2%). Most of the respondents presented that the source of information on Japanese Encephalitis was medical books, course references, and textbooks (47.2%), while 31.7% of respondents provided that their source of information was research articles. However, only 16.9% of respondents demonstrated that their source of information was seminars and workshops, as presented in (Table 2). A possible reason could be the fact that a few workshops and seminars are conducted on rare diseases. It has been proved that seminars and workshops play an important role to enhance knowledge and improve practice (Shahid et al., 2022b).

The majority of the workshops are conducted on the most prevalent diseases to prepare future healthcare professionals for managing the most prevalent diseases. Therefore, the source of information for most of the respondents is medical books. However, a cross-sectional study conducted in Darrang, India presented that most of the respondents presented the source of Japanese encephalitis to be social media and advertisements while only a few respondents had attained knowledge through their family and friends circle (Ahmad et al., 2017). The present study presented that most of the future healthcare professionals (62%) had appropriate knowledge regarding the source, occurrence, and transmission of Japanese encephalitis. However, the medical students (MBBS) presented comparatively better knowledge, while the pharmacy students (PharmD) has the least percentage of appropriate knowledge as compared to Dentistry and Physiotherapy students.

Since, medical students spend a significant amount of time studying pathology, pathophysiology, and clinical medicine (Shahid et al., 2023). It provides them with a deep understanding of various diseases, their mechanisms, and their clinical presentations, which justifies the better knowledge of medical students regarding Japanese encephalitis. In contrast, a cross-sectional observational study conducted on the community population presented low knowledge (24%) of the general population at baseline (Ahmad et al., 2017). In contrast, an observational study conducted in Nepal to evaluate the knowledge of the general community regarding Japanese encephalitis presented poor knowledge at baseline (Keisam et al., 2018). Since the general community has no particular source of information about disease sources and transmission, this justifies the community's low knowledge at baseline.

The current study presented that most of the students (60.2%) presented positive attitudes regarding Japanese encephalitis, among which medical students had the greatest percentage of positive attitudes (71.8%) followed by dentistry, physiotherapy, and pharmacy department students. The possible justification for a better disease management attitude of medical students is because of the enhanced clinical experience and clinical medicine subjects' credit hours. Likewise, another cross-sectional study conducted on future healthcare professionals from Bedong, Malaysia presented somewhat similar results i.e., the majority of the respondents presented a positive attitude at baseline. In a similar manner, the current study has presented good perceptions among the majority of the respondents (60.6%).

However, the perceptions of medical students were more positive as compared to the students of other departments. The possible reason for good perceptions could be the fact that medical students have better disease knowledge, which contributes to good perception. Similarly, the study conducted on future healthcare students from Malaysia presented good practices in response to positive attitudes regarding Japanese encephalitis. The current study presented no statistically significant association of gender with the knowledge, attitude, or practices of the respondents regarding Japanese encephalitis. The possible reason could be the presence of the same curriculum for all the students. The same teaching institute and environment play a significant role in similar professional development of the students (Shahid et al., 2024).

A cross-sectional study conducted in Islamabad, Pakistan presented no association of gender with knowledge of pharmacists (Shahid et al., 2022a). However, the study conducted on Malaysian students presented better knowledge of female students as compared to male future healthcare providers regarding Japanese encephalitis source, prevention, and management. Similarly, an

observational study conducted in China, presented the results of female respondents having enhanced knowledge regarding Japanese encephalitis (Wang et al., 2009). The presence of any healthcare professional in the family is positively associated with enhanced knowledge, attitude, and practices regarding Japanese encephalitis. The presence of healthcare professionals in the family results in enhanced knowledge and practices of the family members due to a constant source of information and guidance (Shahid, 2024).

5. CONCLUSIONS

The present study recruited future healthcare professionals from the final year of medical, dentistry, physiotherapy, and pharmacy departments. The present study presents appropriate knowledge, positive attitudes, and good perceptions in the majority of the respondents. Medical students had the highest percentage of appropriate knowledge, positive attitudes, and good perceptions as compared to dentistry, physiotherapy, and pharmacy students. The gender of the respondent had no significant association. However, the presence of healthcare providers in the family was observed to be statistically associated with appropriate knowledge, positive attitudes, and good perceptions.

Limitations of the study

This study was only conducted in selected educational institutions in Lahore, Pakistan; therefore, the results could not be extrapolated nationwide.

Authors' Contributions

This work was carried out in collaboration among all authors. Authors MZI, SS, FA and MA, designed the study, performed the initial statistical analyses and wrote the protocol. Authors JR, LJ, MZ, SE and SAR collected the data. Authors SS, MC, ZM and MN wrote the first draft of the manuscript. Authors MZI and SS managed refined analyses. Authors FA, MA and SS revised the manuscript. All authors read and approved the final manuscript.

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Ethical Approval

The study was approved by the Medical Ethics Committee of Lahore University of Biological & Applied Sciences, Lahore, Pakistan with the ethical approval number (ERB-PHRMD-DPP/4626-B).

Informed Consent

Written & Oral informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

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Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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